Abstract

Direct C-H borylations of 7-deazapurines (*7H*-pyrrolo[2,3-*d*]pyrimidine) were developed at position 8 using B_2pin_2 and Ir catalysis. The obtained boronates were efficiently applied in the Suzuki cross-couplings with aryl halides and other functional group transformations to give diverse 6-substituted 8-aryl-7-deazapurine derivatives. Furthermore, I was also interested in the synthesis of biologically relevant 8-aryl-7-deazaadenines and -7-deazahypoxanthines. As the direct C-H borylation of 7-deazaadenines was unsuccessful and the borylation/Suzuki reaction of 6-chloro-7-deazapurine gave only low yield (20%) of the desired 8-aryl derivative, I focused on the one-pot borylation/arylation of SEM-protected 6-methylsulfanyl- or 6-methoxy-7-deazapurines. The one-pot borylation/Suzuki coupling reactions were followed either by demethylation and deprotection to yield deazahypoxanthine base, or by oxidation of sulfide to sulfone, amination and deprotection to give deazaadenines. In addition, the boronate intermediates were successfully converted to 8-halo- or 8-trifluoromethyl-7-deazapurine derivatives. While the 7-deazahypoxantine analogues were almost entirely inactive, most of the 8-subtituted 6-methoxy-7-deazapurine and 7-deazaadenines bases showed significant cytostatic activities.

Also a general method for Cu-catalysed C–H sulfenylation of purines, 7-deaza- and 9-deazapurines (*5H*-pyrrolo[3,2-*d*]pyrimidine) with aryl or alkyldisulfides was developed. In purines, the reaction occurs at position 8, in 7-deazapurines at position 7 and in 9-deazapurines at position 9, leading to new interesting arylsulfanyl derivatives of purine or deazapurine bases. The resulting 8-arylsulfanylpurines undergo the Liebesking–Srogl coupling with arylstannanes or boronic acids, whereas the (arylsulfanyl)deazapurines are not reactive under these conditions.

Later on, a series of 7-phenylsulfanyl- or 7-(2-thienyl)sulfanyl-7-deazapurine bases bearing diverse substituents at the position 6 was prepared through C-H sulfenylation of 6-chloro-7-deazapurine followed by cross-couplings or nucleophilic substitutions. The corresponding ribonucleosides (as thia-analogues of known nucleoside cytostatics) were prepared by glycosylation of 6-chloro-7-arylsulfanyl-7-deazapurines followed by the same transformations at position 6. The 7-thienylsulfanyl-7-deazapurine bases exerted micromolar cytostatic activities, whereas the nucleosides showed no significant biological effects.